Remarks

1. Status of the application

Claims 1-26, 55-58 and 65-90 are pending and stand rejected. Claims 4, 12, 15 and 16 are cancelled by this amendment, and new claims 91-93 are added by this amendment. After entry of this amendment, claims 1-3, 5-11, 13-14, 17-26, 55-58, 65-93 are pending.

2. Summary of Examiner's Interview

On April 2, 2003 the undersigned attorney telephoned Examiner Allen to set up a time to discuss the application, and Examiner Allen declined to set up a time unless a compelling reason for an interview after final was presented.

On April 3, 2003, the undersigned attorney left a telephone message for Examiner Allen asking for an interview on the basis that the outstanding Office action contained a new grounds for rejection not necessitated by applicants' response to the first Office action submitted November 5, 2002. Specifically, the undersigned attorney asked Examiner Allen to consider withdrawing the finality of the outstanding Office action because all of the claims were newly rejected under 35 U.S.C. §112, second paragraph for containing the allegedly indefinite term "detecting similarities." The undersigned attorney supported the request for withdrawal of the finality of the Office action by stating that since the allegedly indefinite term appeared in the claims as originally filed, and was not rejected in the first Office action, the grounds for rejection was not necessitated by applicants prior Amendment. [See MPEP 706.07(a)].

On April 4, 2003, Examiner Allen telephoned the undersigned attorney to discuss the finality of the Office action. Examiner Allen stated that other changes made to the claim in the Amendment of November 5, 2002 made it necessary to raise the section 112 rejections in the final Office action. Specifically, Examiner Allen alleged that the rejection could not be made earlier because the significance of the claim term "detecting similarities" could not be appreciated before the Amendment of November 5, 2002.

3. Support for Amendments to the Claims

Support for the amendments to the claims, including independent claims 1, 18, 69 and 82, may be found throughout the application. As clearly stated on page 21, lines 1-2, the methods described in the present application are QSAR [quantitative-structure-activity relationship] methods. As explained

in the Background section of the application, a QSAR is an "attempt to quantify the observed relationships between the structure of chemical compounds between the structure of chemical compounds and the extent to which those compounds exhibit certain properties" (page 2, lines 13-15). As explained at page 2, lines 25-27, "[t]o establish a QSAR, endpoint values are obtained for a set of compounds and a correlation is then sought between the endpoint values and some measure(s) of structure available for each of the compounds." As further explained on page 21, lines 2-3, "the methods [of the present application] utilize spectral data as structure descriptors and correlate the spectral data with specific biological, chemical or physical endpoints." As noted at page 21, lines 8-9, "a correlation provided by the methods ... is termed a Spectral Data Activity Relationship" (page 21, lines 8-9).

As generally explained in the Background at page 3, lines 10-11, "[t]he endpoint data and the structure descriptor(s) for the set of compounds that are chosen to establish a QSAR are termed the training set." As stated generally at page 3, lines 15-16, "[i]f the endpoint and the structure descriptor(s) are sufficiently correlated, a mathematical or graphical representation may be obtained." Further, the application explains at page 3, lines 23-24 that "[t]he QSAR representation may be used to predict endpoint values for other compounds from their structure descriptor(s)." An SDAR, as a special type of QSAR that employs spectral data as structure descriptors, may similarly be established and used to make predictions.

As stated on page 10, lines 10-13, "[i]n other embodiments, spectral data of the training set compounds is segmented into sub-spectral units (bins), and scaled ... prior to pattern recognition." At page 10, lines 14-15, the application states that "[i]n yet other embodiments, the spectral data of the training set compounds is weighted prior to pattern recognition."

A particular embodiment of a method including scaling and weighting of the training set data prior to pattern recognition and establishment of an SDAR, and its use to predict the properties of molecules, is presented on pages 25-28 with reference to FIG. 4. At page 25, lines 10-13, the application states that "FIG. 4 summarizes, in flowchart form, a particular embodiment of the steps that may be taken to establish an SDAR from spectral data," and that "[t]hese steps and others may be performed using a computer system." At page 25, line 14-15 the application states "spectral data is obtained" and "is segmented into bins." The spectral data sets "comprise the structure descriptors for the training set compounds" (page 25, line 20). The application also explains at page 25, lines 24-25 that "[i]n some embodiments, the segmented spectral data is pretreated by autoscaling prior to pattern

recognition." In addition, the application states at page 26, lines 6-7, that "[i]n some embodiments, the segmented spectral data is further pre-treated by Fisher-weighting." At page 27, lines 8-10, the application states that "[p]attern recognition is used to establish an SDAR, by correlating the segmented (and optionally pretreated) spectral data with the endpoint data for the compounds in the training set." At page 27, lines 24-25, the application states that "[p]attern recognition to establish an SDAR may be accomplished by statistical methods or artificial intelligence methods." Pretreatment of spectral data is discussed in Example 8, at page 65, lines 14-15. Here, the application states that "techniques for pre-treating data include ... scaling and weighting."

Establishing an SDAR and using the SDAR to predict the biological activity of a test compound is demonstrated in Example 1. In this example, "[t]wo ... (SDAR) models were established" (page 32, line 15). "The SDAR based on ^{13}C NMR data alone yielded a leave-one-out [LOO] cross-validation of 90% (page 32, lines 20-21)." As explained on page 20, lines 23-29, LOO cross-validation "is a method whereby each compound in the training set is systematically excluded from the data set, after which its endpoint value is predicted by the [SDAR] derived from the remaining compounds," and "[c]ross validation is useful for judging the reliability of a spectral data-activity relationship, especially where a validation set of compounds is not available."

Claim 82 is also supported at page 27, lines 10-14. Here the application states that "[i]n particular embodiments, the compounds are classified into two or more endpoint classes (e.g. strong versus weak estrogen receptor binders) according to their relative endpoint values." Specifically, at page 27, lines 12-14, it states that "[t]he pattern recognition then determines any segmented spectral features (i.e. the bins) that are characteristic of the compounds falling into each of the classes." Working examples of this type of method are provided in Examples 1 and 2 found on pages 31-46.

Support for claim 65 is provided, as discussed in more detail immediately below with respect to the new matter rejections, at page 29, lines 27-29 and at page 30, lines 1-3.

Claims 3, 5, 12, 19, 20, 22, 23, 74 and 83 also have been amended for clarity and to provide proper antecedent basis. Support for claim 23 is provided by the claim itself because no features have been added, rather a feature has been deleted.

Support for new claims 91 and 92 may be found, for example, at page 3, lines 24-25, where the application states that "the reliability of a QSAR may be tested using a validation set of data." On page 21, lines 1-2, the SDAR methods of the application are disclosed to be QSAR methods. Validation is a process that is within the skill of one of ordinary skill in the art, and as discussed in a

following section is the way in which QSAR models are shown to be reliable, i.e. predictive. A validation set and its purpose is discussed on page 17, lines 9-11. Support for "LOO cross-validation" appearing in claim 92 is provided at page 35, line 19 and more generally at page 20, lines 23-29.

Support for new claim 93 may be found, for example, at page 27, lines 23-24, where it states that "[p]attern recognition to establish an SDAR may be accomplished by statistical methods or artificial intelligence methods."

4. Rejections under 35 U.S.C. §112, first paragraph, new matter rejections

Claims 1-17, 25, 55 and 65-90 stand rejected as allegedly containing subject matter that was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants disagree and request withdrawal of these rejections for the following reasons, and in view of the foregoing amendments.

Claim 1, as amended, recites a segmenting step and a scaling step prior to pattern recognition. Since the Office action rejected claim 1 for not including these steps, the rejection of claim 1 under 35 U.S.C. §112, first paragraph, for containing new matter should be withdrawn and applicants request that it be withdrawn.

Claim 69, as amended, no longer recites providing biological activity data since it is implied in the term "training set of compounds having known biological activities." However, biological activity data is nonetheless "provided" in Tables 1 and 2 found on pages 38 and 41-44, respectively, for a training set of data used to establish an SDAR for estrogen receptor binding affinity. Also, claim 69 now recites steps of segmenting the spectral data of the training compounds and segmenting the spectral data of the test compounds. The rejection of claim 69 under 35 U.S.C. §112, first paragraph for containing new matter should be withdrawn and applicants request that it be withdrawn.

Claim 82, as amended, recites "receiving as input training set data, the training data comprising the spectral data and biological activities of a training set of compounds." At page 17, lines 6-8, the application states that the training set is "endpoint data and structure descriptors (structural data) for a group of compounds used to establish a correlation between the endpoint property and the structures of the compounds." On page 57, lines 24-25, the application states that "[e]ndpoints for use with the SDAR methods encompass the full range of biological, chemical, and physical properties exhibited by molecules." Further, at page 57, lines 25-27, the application states that the methods may be used to

assist in "biological activity predictions." Examples of training set data comprising spectral data and biological activities are given in Tables 1 and 2, found at pages 38, and 41-44, respectively. Since the application clearly supports claim 82 as amended, the rejection of claim 82 under 35 U.S.C. §112, first paragraph for containing new matter should be withdrawn and applicants request that it be withdrawn.

Claim 65, as amended, is supported by the application and predicting multiple endpoints (biological activities) of test compounds is clearly contemplated by the application. Contrary to the assertion in the Office action that the basis on "[p]age 29 discloses a discriminant function for a training set split into two endpoints" this portion of the specification supports claim 65. The passage (page 29, lines 27-29) states "[o]nce spectral data are gathered for a set of compounds, an SDAR may be generated with reference to a multitude of biological, chemical, or physical endpoints for which data is available." Continuing at page 30, lines 1-3, an example is given. Here, the application states that "the same set of spectrally derived structure descriptors for a set of compounds may be utilized with toxicity data and antibacterial activity data for these compounds to establish two separate SDARs for compounds, one for toxicity and the other for antibacterial activity." Toxicity and antibacterial activity are biological activities. As stated on page 17, lines 25-27, an SDAR is "useful for among other things for predicting the endpoint data for compounds from their spectral data." Thus, establishment of a second SDAR for a second biological activity that may be used to test a compound for a second biological activity is clearly contemplated by the application. The rejection of claim 65 under 35 U.S.C. §112, first paragraph, for containing new matter should be withdrawn and applicants request that it be withdrawn.

5. *Rejections under 35 U.S.C. §112, first paragraph, non-enablement rejections*

Claims 1-16, 18-26, 55-58 and 65-90 stand rejected for allegedly not providing enablement for methods that do not use a computer. Applicants agree with the statement in the Office action that "the specification [is] enabling for computer implemented methods (page 3, second paragraph)." However, applicants disagree that other methods are not enabled, but nonetheless have amended independent claims 1 and 69 to affirmatively recite the feature of computer implementation, solely to further prosecution. Applicants reserve the right to prosecute broader claims in a continuation application.

Independent claim 18 is directed to "[a] computer implemented method for predicting the biological activity of a test compound." Thus, it is not clear from the Office action why claims 18-26 were rejected for being directed to methods not using a computer. Similarly, independent claim 82 is

also directed to "[a] computer implemented method for predicting the biological activity of a test compound." Again, it is not clear from the Office action why claims 82-90 were rejected for being directed to methods not using a computer.

All of the currently pending claims, as amended, including those that depend from claims 1, 18, 69 and 82, include the feature of computer implementation. Therefore, applicants request withdrawal of the rejections of claims 1-16, 18-26, 55-58 and 65-90 under 35 U.S.C. §112, first paragraph for allegedly being non-enabled.

6. Rejections under 35 U.S.C. §112, second paragraph, indefiniteness rejections

Claims 1-26, 55-58 and 65-90 stand rejected for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants request withdrawal of the rejections for the following reasons, and in view of the foregoing amendments.

Claims 1, 69 and 82 were rejected for reciting the term "detecting similarities," which allegedly fails to make clear how similar patterns of spectral data must be in order to assign or predict that it will have the activity of the training set of compounds, and that it cannot be determined what level of similarity would meet the limitation of the claim. Claim 18 was rejected for reciting the term "similar." Claims 1, 18, 69 and 82, as amended, recite, amongst other features, the features of establishing a spectral data-activity relationship (SDAR) and using the SDAR to predict the test compound's biological activity (or predicting the test compound's activity using the SDAR). As amended, claims 1-26, 55-58 and 65-90 do not use the terms "detecting similarities" or "similar." The rejections of these claims under 35 U.S.C. §112, second paragraph should be withdrawn, and applicants request that the rejections be withdrawn.

Claims 1, 18, 69 and 82 make it clear that it is a relationship between the spectral data and the biological activities of the training set compounds that is established during pattern recognition, and that it is the relationship (model) that is used to predict the biological activity of the test compound from its spectral data. The relationship may be used to provide a prediction regardless of whether the prediction is correct or not, so it is the reliability of the relationship that is important. For example, input of data into a neural network model will yield an output result, but the result may or may not be valid. For this reason, structure-activity models are typically validated to judge their reliability (see, Background, page 3, lines 23-29), for example, by LOO cross-validation (see, page 20, lines 23-39).

Claims 5, 10 and 20 stand rejected as allegedly being indefinite for reciting "substantially the same." Applicants disagree that the phrase "substantially the same" is indefinite. According to MPEP §2173.05(b)(D), the term "substantially" is a broad term. According to MPEP §2172.04, breadth is not indefiniteness. In *Andrew Corp. v. Gabriel Electronics*, 6 USPQ2d 2010 (Fed. Cir. 1998) the court held that the limitation "which produces substantially equal E and H plane illumination patterns" was definite because one of ordinary skill in the art would know what was meant by "substantially equal." Here, it is a pattern of segmentation that is claimed to be substantially the same (or substantially identical), and one of ordinary skill in the art would also know what is meant by "substantially the same." Therefore, the rejections of claims 5, 10 and 20 under 35 U.S.C. §112, second paragraph should be withdrawn, and applicants request that the rejection be withdrawn

Claim 17 was rejected as allegedly indefinite for being confusing. It is submitted that claim 17, as amended, overcomes the rejection. Therefore, the rejection of claim 17 under 35 U.S.C. §112, second paragraph should be withdrawn, and applicants request that the rejection be withdrawn.

7. Rejections under 35 U.S.C. §102

Claims 1-10, 14-15, 18-21, 25-26, 55-58 and 66-68 stand rejected under 35 U.S.C. §102(a) for allegedly being anticipated by Bursi et al. For a claim to be anticipated by a reference, the reference must teach each and every feature of the claim. Applicants disagree that data conversion is scaling. Nonetheless, independent claims 1 and 18 have been amended solely to further prosecution of the application.

Independent claim 1, as amended, which recites the feature of weighting prior to pattern recognition, is not anticipated for at least the reason that Bursi et al. does not teach weighting spectral data prior to pattern recognition. Moreover, claim 1 is not obvious in view of the reference because Bursi et al. does not suggest weighting spectral data prior to pattern recognition.

Claims 2, 3, 5-10 are patentable in view of Bursi et al. for at least the reasons why claim 1 is patentable in view of Bursi et al.

Claim 4 has been cancelled.

Claims 14 is is patentable in view of Bursi et al. for at least the reasons claim 1 is patentable in view of Bursi et al.

Claim 15 has been cancelled.

Claims 55-58 are patentable in view of Bursi et al. for at least the reasons why claim 1 is patentable in view of Bursi et al.

Claims 66-68 are patentable in view of Bursi et al. for at least the reasons why claim 1 is patentable in view of Bursi et al.

Independent claim 18, as amended recites, amongst other features, the feature of weighting the spectral data of the training set of compounds. Bursi et al. does not teach or suggest weighting spectral data. Therefore, claim 18 is not anticipated or rendered obvious by Bursi et al.

Claims 19-21, which depend from claim 18, are not anticipated or rendered obvious by Bursi et al. for at least the reasons set forth in connection with claim 18.

Claims 1-10, 14-15, 18-21, 25-26, 55-58 and 66-68 are patentable in view of Bursi et al. and the rejections of these claims under 35 U.S.C. §102(a) should be withdrawn. Applicants hereby request that these be withdrawn.

All pending claims are ready for allowance, and such action is requested. If any questions remain before issuance of a Notice of Allowance, the Examiner is invited to telephone the undersigned patent attorney at the number give below.

Respectfully submitted,

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